COV

RESEARCH › RESEARCH SUMMARIES

Sharing our progress toward recovery

Research Summaries

Discover what the latest science from the RECOVER Initiative means for our ability to understand, diagnose, prevent, and treat **Long COVID**.

This page contains descriptions of findings from **RECOVER research studies**. These descriptions use plain language and a format that is easy to understand.

If you want to learn more about the scientific discoveries described here, you can also browse and search the complete list of **RECOVER Publications**.

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● EHR ■ ADULT ◆ RISK FACTORS

Risk factors associated with post-acute sequelae of SARS-CoV-2: An N3C and NIH RECOVER study

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information about a person's healthcare. In this study, researchers studied anonymous EHR data from the National COVID Cohort Collaborative (N3C), a group of medical systems located across the United States. They compared a group of 8,325 people who had a Long COVID diagnosis or received healthcare at a Long COVID clinic to a group of 41,625 people who did not have Long COVID. The researchers found key differences between these 2 groups. They also identified risk factors that could make someone more likely to develop Long COVID, including being middle-aged (40 to 69 years old), being female, and having certain chronic (long-term) health conditions before they got COVID. Examples of these chronic health conditions were obesity and lung disease. More research is needed to better understand why and how the risk factors found in this study make someone more likely to develop Long COVID.

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REVIEW ADULT

The importance of patient-partnered research in addressing Long COVID: Takeaways for biomedical research study design from the RECOVER Initiative's Mechanistic Pathways taskforce

Kim, C; Chen, B; Mohandas, S; et al., *eLife*

Long COVID patients, caregivers, and community members contribute to all parts of RECOVER, including scientific research. These chosen members of the community are known as RECOVER Representatives. This paper, written by a team of RECOVER Representatives and researchers, talks about why they chose to work together and how their partnership has improved the study. They summarize some of the impacts of Long COVID and highlight the roles that patient advocacy can play in research.

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to include patients, and sharing community concerns has set a new example for the design of future biomedical research studies.

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EHR ADULT NEW-ONSET AND PRE-EXISTING CONDITIONS RISK FACTORS

Risk of post-acute sequelae of SARS-CoV-2 infection associated with pre-coronavirus disease obstructive sleep apnea diagnoses: An electronic health record-based analysis from the RECOVER Initiative

L Mandel, H; Colleen, G; Abedian, S; et al., *Sleep*

Researchers wanted to see if patients who had difficulty breathing while sleeping (Obstructive Sleep Apnea; OSA) were at higher risk for developing Long COVID compared to people without OSA. By comparing the electronic health record (EHR) data of COVID positive patients, researchers looked at the risk of developing Long COVID in patients with and without a previous diagnosis of OSA.

Researchers found that adults with a previous diagnosis of OSA had an increased chance of developing Long COVID when compared to patients that did not have a previous diagnosis of OSA.

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EHR PEDIATRIC

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Lorman, V; Razzaghi, H; Song, X; et. al., *PLOS ONE*

To understand Long COVID, researchers must be able to figure out which patients have it. Our understanding of Long COVID is evolving and it has been difficult to know who had Long COVID, especially in children. We need a reliable method to identify who might have Long COVID using existing health data.

The purpose of this study was to create and test a computer program, called an algorithm, to find out which children have Long COVID based on their electronic health records (EHRs). EHRs (digital medical charts that have health data like doctor visits, lab results, and other health history) are an important source of data for research studies on Long COVID. The algorithm looks at EHRs to find patterns in the diagnoses, prescribed medications, procedures, and lab tests children received after having COVID-19. These patterns can be described as a phenotype, or a set of measured or visible traits, that can tell us who had Long COVID.

The algorithm correctly identified 67% of the patients who had a Long COVID diagnosis from the EHRs. Among the patients who the algorithm said had Long COVID, 91% had a Long COVID diagnosis. Overall, the algorithm was correct in identifying whether a patient had a Long COVID diagnosis 99% of the time. This means the phenotype can be used to recognize which children have Long COVID in EHR data for future studies, or to screen patients to participate in clinical trials.

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● EHR ■ ADULT ◆ HEALTH DISPARITIES

◆ NEW-ONSET AND PRE-EXISTING CONDITIONS

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Yoo, YJ; Wilkins, KJ; Alakwaa, F; et. al.; N3C and RECOVER Consortia, *Clinical Journal of the American Society of Nephrology*

Acute Kidney Injury (AKI) can happen when people get very sick with COVID-19. People in the hospital with COVID are more likely to die if they also get AKI. However, there is not enough research to understand how many people have had AKI since the start of the COVID pandemic or what increases the chances of getting AKI. In this RECOVER study, researchers looked at the electronic health records (EHRs) from 53 hospitals across the United States. They studied adults who were in the hospital with COVID between March 2020 and January 2022. To find out who had AKI, the researchers looked at blood tests that show how well the kidneys are working and diagnosis codes (what doctors use to say what's wrong with the patient). To understand where people were getting sick, researchers split the country into 4 parts: Northeast, Midwest, South, and West. They also looked at different time periods during the pandemic. Out of 336,473 people in the study, 129,176 (38%) had AKI. People with AKI were also more likely to die than those without AKI. The South and the West had the most cases of AKI. Researchers found that AKI cases went down after the first big wave of COVID, but then went back up during the Delta and Omicron waves. This shows that different types of COVID might affect the kidneys differently. This study is important because it helps us understand how COVID can hurt people's kidneys, and how it can change over time. It also helps us learn how COVID is linked to things like age, sex, race, and other health problems in different areas of the country.

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● EHR ■ PEDIATRIC

Leveraging serologic testing to identify children at risk for post-acute sequelae of SARS-CoV-2

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To find another way to know if children had COVID, researchers compared health records of 2 groups of children: children who only had a positive antibody test and children who had a positive PCR test. A **positive antibody test** means a child had COVID in the past, had the COVID vaccine, or both. A **positive PCR test** means a child currently has COVID. Researchers used data from children's hospitals in the National Pediatric Learning Health System (PEDSnet) network.

Antibody tests found 2,714 children who had COVID and didn't have a positive PCR test or COVID vaccine. If researchers used only PCR tests, they wouldn't have known these children had COVID. Knowing if children had COVID is the first step to know their risk of Long COVID and if symptoms could be related to Long COVID.

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OBSERVATIONAL ADULT

Researching COVID to enhance recovery (RECOVER) adult study protocol: Rationale, objectives, and design

Horwitz, LI; Thaweethai, T; Brosnahan, SB; et al., *PLOS ONE*

A COVID-19 infection can lead to new symptoms or symptoms that do not go away. This condition is called Long COVID. RECOVER researchers are working to answer questions about Long COVID in adults. To do this, they are studying over 12,000 adults in the US to understand how common Long COVID is in adults; how the body changes when someone has Long COVID; what makes some people more likely to develop Long COVID, such as where a person lives and their age, race, and sex; and what

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OBSERVATIONAL ADULT BROAD SYMPTOMS
HEALTH DISPARITIES NEW-ONSET AND PRE-EXISTING CONDITIONS

Development of a definition of Postacute Sequelae of SARS-CoV-2 infection

Thaweethai, T; Jolley, SE; Karlson, EW; et al., *JAMA*

RECOVER researchers used data from the RECOVER observational cohort study in adults ages 18 and over. They compared symptoms reported in surveys by participants who did and did not have COVID.

Researchers found 37 symptoms that participants who had COVID reported more often after having COVID compared to participants who never had COVID. 12 of these symptoms could identify participants with Long COVID, including feeling tired and unwell after activity, feeling weak and tired (fatigue), and brain fog. A definition of Long COVID based on symptoms is important for future research, including to find treatments.
Read the Research Q&A →

Research Summary (PDF, 129 KB)

Resumen de la investigación (PDF, 182 KB)

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RISK FACTORS

De-black-boxing health AI: Demonstrating reproducible machine learning computable phenotypes using the N3C-RECOVER Long COVID model in the All of Us data repository

Pfaff, ER; Girvin, AT; Crosskey, M; et al., *Journal of American Medical Informatics Association*

A quick way for scientists to identify patterns in a large set of data is by teaching computers to find those patterns for them. To do this, the scientist creates a set of instructions for a computer to follow, called an algorithm, to locate exactly what the scientist is looking for. When that algorithm is plugged into a software program, a computer can run the algorithm many times and learn from it. This process improves the algorithm and it becomes more accurate over time. This is called machine learning. Machine learning can be very helpful and accurate, but it is also challenging to share between researchers because each computer can learn things on its own that can be difficult to recreate. When a computer arrives at an answer that a scientist cannot recreate, it is known as a black-box algorithm.

In order for one research team to share their findings with another research team, they must be able to recreate the steps of the algorithm to “de-black-box" it. This was done by researchers from the National COVID Cohort Collaborative (N3C) as part of the National Institutes of Health (NIH) RECOVER Initiative. The N3C team first identified a phenotype (measured or visible traits) for patients who were at a higher risk of developing Long COVID by creating and training a machine learning-based algorithm. Then, with RECOVER’s support, the N3C researchers worked with researchers from another NIH study called *All of Us*. They were able to re-create the machine learning-based algorithm, leading to the same phenotype. This means that they were able to “de-black-box" their algorithm. This case can be used as a guide of best practices when sharing algorithm data between research teams. This way,

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